frequently, reaching subnormal 95° to 97°. Cardiac stimulants were given freely, strychnin, sodium caffein benzoate, digitalis, strophanthus; an ice-bag was placed at the head and chipped ice was given by mouth. For subnormal temperature external heat was applied. For recurrences in temperatures up to 103° cold packs and alcohol sponges were given; above 103° the patient was again given a cold water friction bath. It was observed that recurrent temperatures could not be reduced as easily as the initial high temperature, and in a few instances the temperature continued to rise in spite of prolonged friction in cold water. For restlessness and convulsions sedatives were used; morphin, chloral hydrate, scopolomin, the bromids, and mechanical restraints.

AN ELECTROCARDIOGRAPHIC STUDY OF A HEART SHOWING ECTOPIC AURICULAR CONTRACTIONS, WITH SPECIAL REFERENCE TO THE INFLUENCE OF THE VAGUS NERVES ON THE ECTOPIC FOCUS.

By Drew Luten, M.D.,
ST. LOUIS, MO.

(From the Department of Internal Medicine, Washington University.)

That the vagus nerves influence the rhythmicity, contractility, conductivity, and irritability of the heart is well known, but it seems probable that the two nerves do not exercise the same influence over the various cardiac properties, at least not in the same degree. The idea is gaining ground that the specialized tissues are more richly supplied with vagus fibers than the main mass of cardiac muscle, and that it is to the distribution of the two nerves that their specific action is due. There is evidence for the belief that the specialized tissue in the region of highest rhythmicity—that is, the right auricular sinus—is supplied mainly by the right vagus; while the specialized tissue between the auricles and ventricles that conducts the impulse downward, receives its nerve supply mainly from the left vagus. The latter, therefore, exercises a greater influence over conduction, just as the right vagus has the greater control over the heart rate. The extent to which the vagi supply the undifferentiated portions of the heart muscle is not so well understood. Cases showing vagus influence on ectopic beats are very rare. Whether this is because such beats usually arise outside the specialized tissues cannot be decided at present. The case forming the basis of this paper shows a vagus influence upon the occurrence of beats that arise in an ectopic focus of stimulus production, and is thought worthy of record for that reason. It is

also an example of an unusual type of constant arrhythmia, and it shows how a study of the time relationship between a premature auricular contraction and the normal ventricular systole may be important in determining the cause underlying the varying effect of the ectopic beats upon ventricular activity. It records, furthermore, a change in the form of the normal auricular complex apparently due to vagus influence.

The patient whose electrocardiographic records have been studied exhibited cardiac arrhythmia a year or more before his admission to the Barnes Hospital, during an examination for insurance, at which time it was observed that his pulse was bigeminal. The illness for which he was admitted to the hospital, diagnosed influenza, apparently therefore had no relation to his cardiac abnormality. He had gonorrhea three years before his admission. There is no history of other infectious disease. He had had some dizziness, weakness, and palpitation of the heart for several years, and is of the type commonly called "neurotic." At no time has there been any evidence of impairment of the functional efficiency of the heart, nor has physical examination revealed signs of an organic lesion.

Electrocardiograms have been obtained at intervals over a period of ten months. Throughout all of the records an abnormal auricular wave occurs at varying intervals. In lead I this is seen as a small notch on the terminal portion of the ventricular complex of the preceding beat, and in leads II and III it has the form of a downwardly deflected wave in the same position (Fig. 1). This abnormal wave, designated *P'* in the records, is followed at times by a normal ventricular complex; at times it occurs alone, and at other times an abnormal or aberrant complex follows it.

The auricular contraction then which the abnormal wave represents arises in some abnormal focus of stimulus production and occurs prematurely, the contraction taking place before the preceding normal systole of the ventricles is complete. At times this premature auricular[1] contraction sets up a normal contraction of the ventricles, at times it causes no ventricular response, and at other times the response of the ventricles is abnormal or aberrant. It was to seek the explanation of these phenomena, as well as the explanation of the irregular occurrence of the ectopic beat, that this study was undertaken.

It was found that the ectopic focus of stimulus production was under the control of the vagi and the extent and character of this control were studied in numerous electrocardiograms. Curves were made also so as to record the effect of paralysis of the vagus terminations by subcutaneous injections of atropin, to show the

[1] The ectopic beats are referred to as auricular beats; whether indeed the focus whence they arise is in the lower zone of the auricle or in the higher levels of the junctional tissues is perhaps a matter of some question.

effect of exercise and of stimulation of the vagi by pressure over the nerves in the neck.

The patient was given $\frac{1}{36}$ grain of atropin subcutaneously on several occasions, and the resulting behavior of the heart, as recorded in the electrocardiograms, was always the same. The rate was slowed at first, due to the well-known stimulating effect of atropin

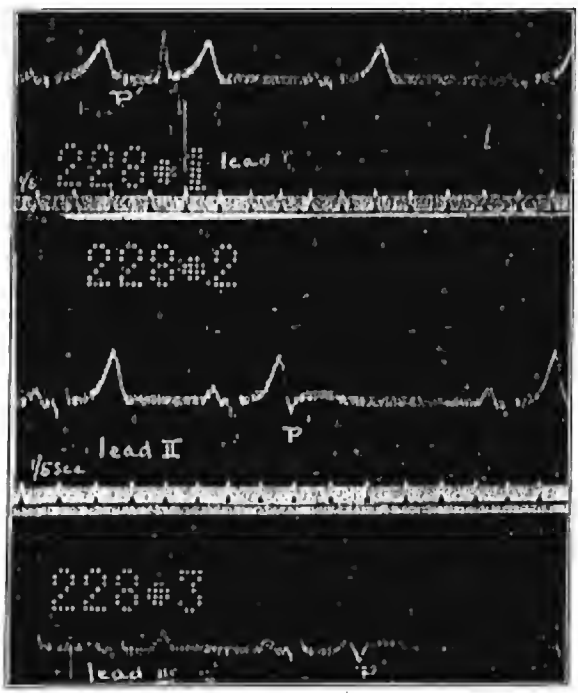

FIG. 1.—Electrocardiograms showing the abnormal *P* wave in all three leads.

on the vagus terminations soon after injection. The ectopic auricular contractions did not occur during this period of vagus stimulation, but as the rate began to increase the ectopic beats became more and more frequent, and finally they occurred regularly at one-third the rate of the pace-maker.

These and other details of the effects of atropin on the heart

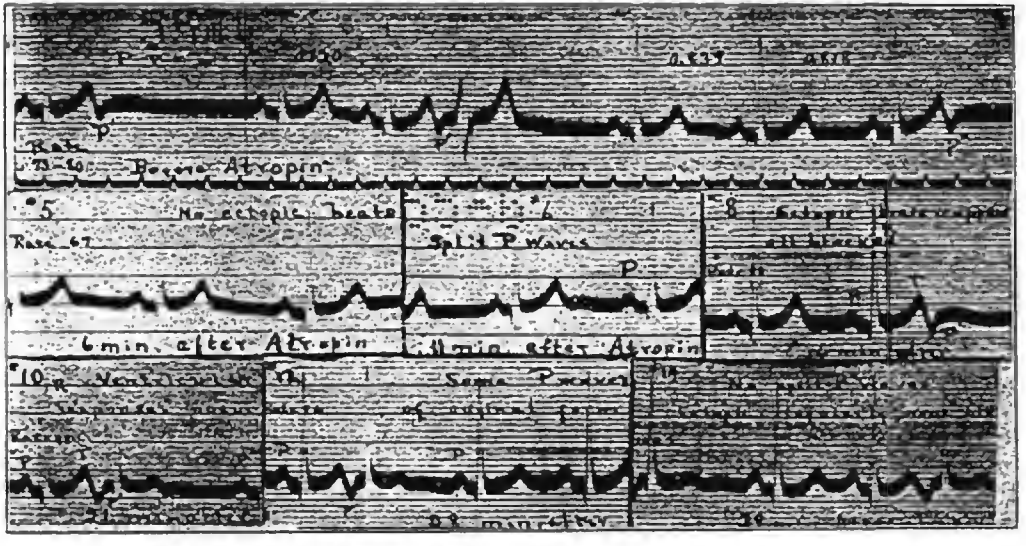

FIG. 2.—Electrocardiograms obtained during the first atropin experiment. The record obtained before atropin injection shows an aberrant ventricular complex following a negative *P* wave. Records were numbered in order and some are not reproduced. (See Table I.)

during two experiments are given in tabular form, the phenomena that show the effects on the auricular activity being shown in the first column; the time and accompanying effects during each experiment, in the other columns. The results of two experiments are recorded. In the first column under each experiment is given the time elapsing between the injection of atropin and the recording of the auricular phenomenon mentioned in the large column at the left of the table. The records were taken at intervals of from two to five minutes, and show, therefore, only approximately the time after atropin at which the various phenomena appeared. The figures in the second small column refer to the numbers of the curves taken during the experiment. In the third column is recorded the rate per minute as estimated from the average interauricular interval. The fourth column gives the auriculoventricular conduction time. The fifth column gives the time elapsing between the onset of the normal ventricular systole and the occurrence of the ectopic beat of the auricles. Since the beginning of the *P'* wave cannot be determined because of its blending with the preceding *T* wave, a constant point on the *P'* wave is used for the measurements. The point selected is the near point of the lowest part of the *P'* wave, and the figures given are therefore not a measure of the true *R–P'* time, but serve just as well for comparative observations. The sixth column measures the duration of ventricular systole. (Here again the figures are not absolute, the crest of the *T* wave being selected as a constant point.) The last column gives the *P'–Q'* time. (This is measured from the beginning of the horizontal portion following the *P'* wave, and to this is added in the earlier curves the length of the *P'* wave as measured in the later curves.)

TABLE I.—EXPERIMENT 55. BEFORE ATROPIN. ECTOPIC BEAT AFTER EVERY TWO OR THREE NORMAL BEATS. NEARLY ALL BLOCKED.

Effect of atropin gr. 1/30 hypo on auricular activity.	Time after injection.	Curve No.	Rate per minute.	Conduction, average P–Q time seconds.	Average R-P' time seconds.	Average R-T time seconds.	Average P'-Q' time.
	Before	4	73-80	0.161	0.355	0.295	0.216
Ectopic beats disappear	6 min.	5	67	0.161			
Slowed rate	11 "	6	66	0.151	....	0.286	
Appearance of "split" P waves	11 "	6					
Ectopic beats reappear—blocked	16 "	8	83	0.111	0.318	0.292	
Ectopic beats continue, all blocked	18 "	9	79	0.111	0.310	0.289	
Some ectopic beats followed by ventricular response	21 "	10	88	0.101	0.309	0.281	0.190
Some P waves of original form appear	28 "	12	96	0.117			
Disappearance of "split" P waves	39 "	11	101	0.110			
Ectopic beats appear regularly after every 2 normal beats. None blocked	30 "	14	104	0.116	0.311	0.250	0.179
Fastest rate	55 "	17	108	0.118	0.356	0.213	
Last record after atropin	50 "	17	....	....	....	....	0.178

TABLE II.—EXPERIMENT 228. BEFORE ATROPIN. ECTOPIC BEAT AFTER EVERY TWO TO SIX NORMAL BEATS. VERY FEW BLOCKED.

Effect of atropin-gr. 1/30 hypo. on auricular activity.	Time after injection.	Curve No.	Beats per minute.	Conduction, average P-Q time seconds.	Average R-P' time seconds.	Average R-T time seconds.	Average P'-Q' time.
	Before	2	56-65	0.155	0.360	0.290	0.291
Ectopic beats disappear	9 min.	11	56	0.119			
Slowest rate	9 "	11	56	0.149	....	0.295	
Appearance of "split" P waves	9 "	11					
Ectopic beats reappear—blocked	10½ "	12	70	0.151	0.359	0.291	
Ectopic beats continue, all blocked	11 "	13	78	0.150	0.359	0.292	
Some ectopic beats followed by ventricular response	16½ "	14	78	0.150	0.356	0.281	0.201
Some P waves of original form appear	28 "	17	92	0.159			
Disappearance of "split" P waves	28 "	17	92	0.159			
Ectopic beats appear regularly after every 2 normal beats. None blocked.	28 "	17	92	0.159	0.372	0.250	0.179
Fastest rate	48½ "	20	101	0.161	0.397	0.235	0.149
Last record after atropin	60 "	23	101	0.156	0.401	....	0.133

In the first atropin experiment (experiment 55, Table I; Fig. 2), before the injection the normal auricular rate was 75 to 80 per minute, and the ectopic auricular beats were occurring, in their usual position, after every two or three normal beats of the auricles. Very few of the ectopic beats were followed by a contraction

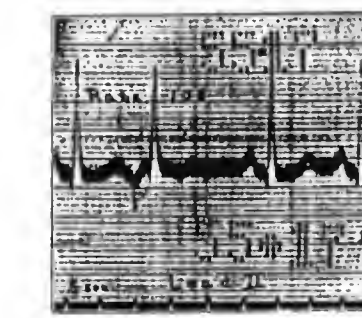

FIG. 3.—Electrocardiogram obtained during the first atropin experiment at the height of vagus paralysis. Negative *P* waves occur regularly and frequently, and all are followed by ventricular complexes.

of the ventricles. Soon after the injection of atropin a moderate slowing of the heart-rate occurred, as is generally observed, due apparently to a stage of vagus stimulation which precedes paralysis. During this period of slowing, at about six minutes after injection, the ectopic beats disappeared, and a little later the form of the normal auricular complex changed, becoming bifurcated. At

sixteen minutes after the injection the stage of vagus paralysis had begun, as indicated by an increase in the rate to 83 per minute. At this time some of the ectopic auricular beats reappeared, occurring at irregular intervals, but none were followed by a response of the ventricles. At twenty-one minutes some ectopic beats began to stimulate ventricular contractions, and at thirty-nine minutes, when paralysis was so far complete as to cause a rate of 101, an ectopic auricular beat was occurring regularly after every second normal auricular beat, and each was followed by a response of the ventricles. This continued, with further increase in rate, to the end of the experiment (Fig. 3).

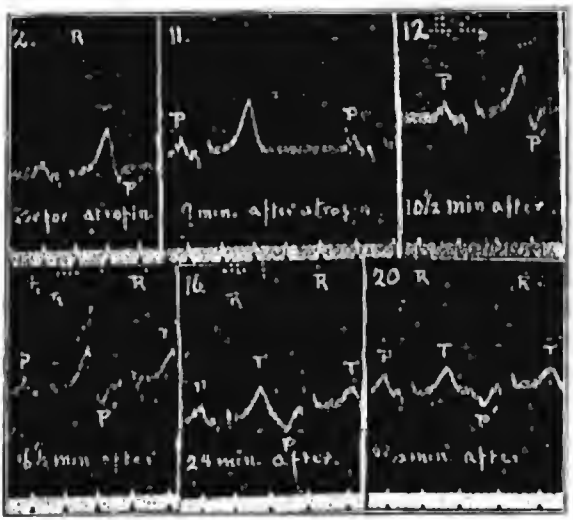

FIG. 4.—Electrocardiograms obtained during the second atropin experiment. Figures on the records refer to the table. Ventricular responses occur in Nos. 14 to 16, when the *R-T* time begins to shorten, though there is, as yet, no increase in *R-P''* time.

In the second atropin experiment (experiment 228, Table II; Fig. 4) before the injection the ectopic beats were occurring less frequently than in the first experiment, and almost all were followed by ventricular contractions. Notwithstanding this difference in the relative frequency of the ectopic beats, and the greater frequency with which they were stimulating the ventricles to a contraction, their behavior under atropin paralysis was practically

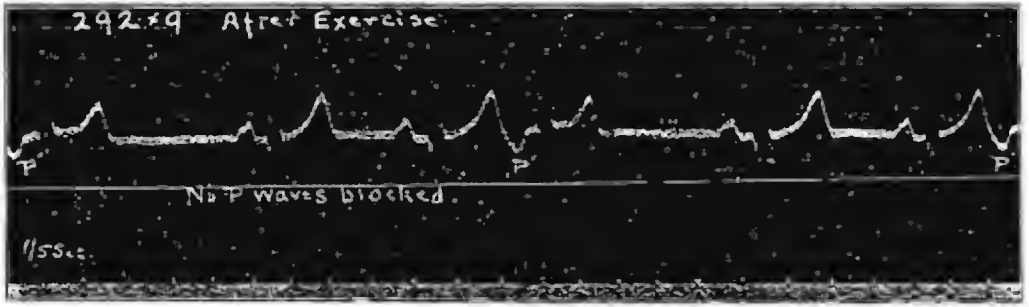

FIG. 5.—After exercise. Rate 75. Negative *P* waves occur regularly after every second normal auricular complex. All are followed by ventricular complexes.

identical with that in experiment 55. In the early period of vagus stimulation they disappeared; with the increase in rate as vagus paralysis began to manifest itself they reappeared at intervals, without stimulating at this time contractions of the ventricles. And later, under more complete atropin effect, they occurred regularly after every second normal beat, all at this period causing ventricular responses. It is worthy of mention that with the increase in vagus paralysis the "split" form of the normal auricular wave began to disappear, and finally at the time of the regular occurrence of the ectopic beats, when vagus paralysis was quite extensive, the normal form of the auricular wave was the only one occurring.

Besides the usual acceleration, three features then are worthy of comment in discussing the effect of atropin on the heart-beat of this patient: (1) the changes in the frequency of the ectopic auricular contractions; (2) the varying manner in which these impulses affect ventricular activity; (3) the alternation in the form of the complex yielded by the normal auricular contractions.

It was observed that the effect of atropin on the occurrence of the ectopic auricular beats was the same in the two experiments, though their relative frequency differed before the administration of atropin. For the first few minutes, during vagus stimulation, the normal pace-maker was depressed and the rate was slowed. This stimulation of the vagus was active at the ectopic focus also and the abnormal waves disappeared. As the stimulation began to give way to vagus paralysis the normal beats increased in frequency and the abnormal contractions also began to appear. Both increased in frequency until the vagus terminations were completely under the influence of the atropin, at which time the normal rate had been increased thirty-five or forty beats per minute, and the ectopic focus was initiating regularly every third auricular contraction. It appears, therefore, that the vagi influence the rate of stimulus formation at the ectopic focus as well as the rate of stimulus formation in the normal pace-maker. When the latter is slowed by vagus stimulation the ectopic focus also is depressed and fails to generate impulses; and when the pace-maker is freed of vagus control and the normal rate increases, the ectopic focus also initiates contractions regularly at as high a rate as 36 per minute.

The manner in which the ectopic impulses affect ventricular activity also is subject to the same variations in the two experiments, as was pointed out above. During the time of vagus stimulation the ectopic beats do not occur, and a little later, when vagus paralysis is increasing, as indicated by the increase in rate, these beats appear; but at this time none of them stimulate the ventricles to respond. Later, with the increase in rate, occasional responses of the ventricles occur, and still later all of the regularly occurring ectopic beats are followed by contractions of the ventricles.

The cause of this variation in the manner in which the ectopic beat affects ventricular activity is not easy to determine. In seeking an explanation of this phenomenon several questions arise for consideration: Is the path of the ectopic impulse to the ventricles the seat of some conduction defect? Does the premature beat, at the period when no ventricular responses follow it, occur so closely following the normal beat of the auricles that the bundle has not had time to recover sufficiently by the time the premature beat reaches it to conduct the ectopic impulse to the ventricles? Does atropin improve conduction in the path taken by the ectopic impulse to such an extent as to overcome any such hindrance as may be present? Does the ectopic impulse upon its arrival at the ventricles find the latter still refractory from the normal contraction that has just occurred, and on this account, unable to beat again in response to the ectopic impulse?

An extended discussion of these various possible factors and the part each may play in the behavior of the ventricles following the ectopic impulse would lead too far afield. It may be pointed out, however, that the conduction time of the abnormal impulse, the *P'-Q'* time, decreases under atropin, as shown in the tables. On the other hand, strips of a long record when no atropin has been administered may show many ectopic beats accompanied by ventricular responses and many others that cause no response of the ventricles. There is no constant relationship in records taken under atropin or in those without atropin, between the time relationship of the premature beat to the preceding ventricular systole. This *R-P'* time varies slightly, but in no constant way as related to the presence or absence of ventricular complexes. A study of the tables shows that ventricular responses occur at those times when the period of ventricular systole, as estimated by the *R-T* time, is short. This occurs with increase in rate, and may be the chief factor in allowing a response of the ventricles to the ectopic beat. With a shorter ventricular systole the refractory phase of the ventricles passes off more quickly, and an impulse from above, though reaching them in the same absolute time interval, would find the ventricles in a later phase and sooner ready to contract again. A careful study of many records shows that the faibre of the ventricles to respond to the ectopic auricular beat always occurs with a change to a slower rate; and with the slower rate, ventricular systole is, of course, prolonged. When the rate is fast, following atropin administration, exercise or sinus arrhythmia, the premature beats succeed in stimulating the ventricles to respond.

Whether any one factor can be regarded as the only or indeed as the chief influence in producing ventricular responses to the ectopic beats is perhaps an open question. Whatever the cause, however, the same influences probably operate to produce the aberrant complexes. These occur both under atropin and in

curves when no atropin has been administered, when the rate is intermediate between that rate at which no responses of the ventricles follow the premature beats and the rate at which all premature beats produce responses of the ventricles that are of approximately normal form. At these times apparently a ventricular contraction occurs before the refractory phase has passed off entirely or before the *a-v* bundle has recovered, as the case may be, and contractions yielding abnormal or aberrant ventricular complexes take place. According to Robinson[2] the abnormal form of the *Q*, *R*, *S*, group of the ventricular complex is caused by incomplete recovery of the intraventricular conducting system. He believes that the impulse reaches the ventricles when the intraventricular conducting system is in a state of functional fatigue, so that the passage of the impulse through the ventricles does not take place in a normal manner.

The point to be emphasized in considering the influence that the injection of atropin had on the relation of the ectopic auricular impulses to ventricular activity is the fact that certain factors other than a change in conduction may be important in causing the failure of the ventricles to respond to the ectopic impulse. The time relationship of the ectopic auricular impulse to the refractory phase of the ventricles must always be borne in mind when considering the failure of premature impulses to cause ventricular response, and the production of aberrant ventricular complexes. This time relationship may be modified by the earlier or later occurrence of the ectopic beat as has been pointed out by Lewis[3] or the determining factor may be a change in the duration of ventricular systole.

The electrocardiograms obtained following the administration of atropin show a change in the form of the waves yielded by the normal auricular contractions. This change consists of a splitting of the *P* wave, which appears during the period of vagus stimulation and passes off when vagus paralysis becomes established. Changes similar to these have been discussed by Meek and Lyster[4] and by Weil,[5] who consider that the alteration in the form indicates a depression in sino-auricular conduction, and regard the split waves as a record of sinus and auricular activity separated from one another. The possibility that this splitting indicates a displacement of the point of origin of the impulse must also be con-

[1] Arch. Int. Med., 1916, xviii, 830, The Relation of Changes in the Form of the Ventricular Complex of the Electrocardiogram to Functional Changes in the Heart.

[2] Heart, 1910, ii, 23, Galvanometric Curves Yielded by Cardiac Beats Generated in Various Areas of the Ventricular Musculature. Heart, 1912, iii, 279. Observations upon Disorders of the Heart Action.

[4] Am. Jour. Physiol., 1914, xxxiv, 368, Experiments on the Origin and Propagation of the Impulse in the Heart, etc.

[5] Deutsch. Arch. f. klin. Med., 1914, cxvi, 186, Beiträge zur klinischen Elektrokardiographie.

sidered. The significance of the splitting of the *P* wave under the influence of atropin will not be discussed further at this time.

It has been seen that when the rate of the pace-maker is slow during vagus stimulation in the early phase of atropin action, the ectopic focus also is depressed and the premature beats do not occur; and when the normal rate later is increased with atropin paralysis the ectopic beats also occur more frequently and quite regularly. The same phenomenon is observed accompanying an increase in rate with exercise. A record obtained before exercise shows the pace-maker initiating normal auricular contractions at the rate of 58 per minute, and an ectopic contraction occurring after every third normal beat. After exercise (Fig. 5) the rate of the normal auricular impulses had increased to 75 per minute and the rate of the ectopic beats also had increased so that one of these occurred after every second normal beat. During this period of increased rate all the ectopic beats were followed by ventricular responses, while before exercise, with the slower rate, very few were stimulating the ventricles to respond.

Stimulation of the vagi by pressure over the carotid artery, either on the right or left side of the neck, was done on several occasions. The heart-rate was usually moderately slowed by pressure on either side. On two occasions, once with right and once with left vagus pressure, the ectopic beats disappeared with a coincident slowing of the auricular rate. Although this phenomenon was not constant its occurrence strengthens the belief gained from the atropin experiments that the rate of ectopic stimulus formation was under the control of the vagi as well as the rate of stimulus formation in the normal pace-maker. This belief is still further strengthened by observing the behavior of the ectopic focus accompanying changes in vagus tone as indicated by sinus arrhythmia. Wherever changes in the relative frequency of the ectopic beats occur, parallel changes in vagus tone at the sinus are indicated by a change in the rate of the normal auricular beats.

On one occasion pressure over the right vagus caused a prolonged cessation of impulse formation in the normal pace-maker, and allowed some other point in the auricles to initiate contractions which yielded negative *P* waves (Fig. 6). The form of these negative waves differs somewhat from that of the usual ectopic beats,[6] which makes it seem probable that the impulse to the contractions which produced the two waves was initiated at some new focus. The occurrence of the next ectopic beat of usual type sequentially and so closely after the second negative wave in question strengthens this belief. The following ectopic beat of usual type (*P'*) occurs after only one normal auricular beat, the sequence having been

[6] The form of these waves unmodified by the preceding *T* wave can be seen in the latter part of Fig. 4.

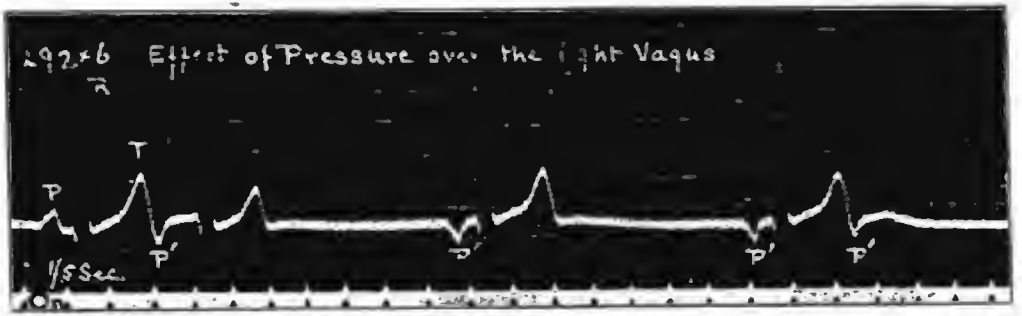

FIG. 6.—Electrocardiogram obtained during right vagus pressure. In two instances the normal auricular complexes are replaced by abnormal waves.

FIG. 7.—Electrocardiogram showing the mingling of the negative *P* wave and the normal auricular complex.

disturbed by a change in the vagus tone at the normal and ectopic areas due to vagus pressure. The point to be emphasized is that here, as elsewhere, there is manifested the influence of the vagus over the ectopic focus as well as over the sinus area. It may also be observed that here too the ectopic impulses fail to cause ventricular responses during the slow rate.

One phenomenon of interest that has not been mentioned was presented by this case during the second atropin experiment (No. 228). In Fig. 4 and in the table it is observed that when the ectopic beats began to occur regularly after every second normal beat, that is, when the vagus paralysis had become fairly well established, the time interval from the beginning of ventricular systole to the occurrence of the ectopic beat began to lengthen. In other words, the ectopic beats become further and further removed from the normal beats of the auricle preceding, until finally this time interval was nearly the normal interauricular interval and the ectopic beat occurred at about the time of the normal beat of the auricle (Fig. 7). When this took place the two contractions (whose stimuli arose in different foci) occurred together, one yielding on the record an upwardly directed wave, the other a wave directed downwardly; and the resulting record shows a small, irregular, in places almost iso-electric complex.

The constant relation of the ectopic auricular wave to the *T* wave of the preceding normal ventricular complex and the disturbance of this relationship under atropin paralysis are interesting features of this case. A discussion of the cause of this relationship, however, involves many hypothetical considerations, and will not be entered upon at this time.

SUMMARY. A case of cardiac arrhythmia caused by almost constantly occurring ectopic auricular contractions is described. The case has been studied especially in order to determine what influence the vagus nerves might have on the ectopic focus of stimulus production.

It has been found that stimulus formation in the ectopic focus is under the control of the vagi as well as in the normal pace-maker of the heart. The ectopic beat is inhibited when the vagus activity is increased, and occurs frequently and regularly when the vagus activity is lessened or removed. This fact has been observed by the study of electrocardiographic records made before and after atropin administration, exercise, and stimulation of the vagi by pressure. Changes in vagus influence at the ectopic focus accompanying sinus arrhythmia lead to the same conclusion. There is no conclusive evidence that the ectopic focus is under the control of one nerve more than the other.

The study of this case also emphasizes the fact that the time relationship of the ectopic beat to the preceding ventricular con-

traction may be an important factor in determining whether or not the ectopic beat of the auricle will stimulate the ventricle to contract, and whether this contraction of the ventricle caused by the ectopic auricular beat will yield a normal or aberrant complex in the electrocardiogram. Other factors than conduction changes may be important in this relationship, and the shorter time occupied by ventricular systole as the heart-rate increases, causing the refractory period to end sooner than it does when the rate is slow, is suggested as a factor in this case in allowing the ectopic beats to stimulate contractions of the ventricles when the rate is fast and not to cause ventricular responses when the rate is slow.

This case shows a splitting of the *P* wave of the electrocardiogram during periods of increased vagus activity which may be interpreted as due to a change in the location of the pace-maker. A record of auricular activity arising synchronously in two separate foci is shown.

The case seems worthy of record because it demonstrates that the vagi may be active upon an abnormal focus of stimulus formation. This vagus activity influences stimulus production in the ectopic focus as well as in the normal pace-making area of the heart.

I wish to express my appreciation of Dr. Robinson's unfailing interest and assistance in the study of these records, and to thank him for helpful suggestions in trying to arrive at a proper interpretation of them.

ETIOLOGICAL FACTORS OF ACNE VULGARIS.

By Albert Strickler, M.D.,

ASSISTANT DERMATOLOGIST TO THE PHILADELPHIA GENERAL AND SAMARITAN HOSPITALS; INSTRUCTOR IN DERMATOLOGY IN PHILADELPHIA POLYCLINIC AND COLLEGE FOR GRADUATES IN MEDICINE.

Although acne vulgaris is one of the most common of all cutaneous affections, yet the etiology of this disease has received insufficient attention at the hands of the dermatologists and practitioners.

Acne while not causing physical suffering, as a rule, may occasion an amount of mental distress and annoyance which is to some almost unbearable, and while it never endangers life it may often and does render existence so miserable that some individuals badly afflicted with it have even wished to die.

Statistics regarding the frequency of acne will vary, dependent upon the sources from which they are obtained.